

December 20, 2002

Lorraine E. Twerdok, Ph.D., DABT
Manager, Health Sciences
American Petroleum Institute
1220 L Street, N.W.
Washington, DC 20005

Dear Dr. Twerdok:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for the Waxes and Related Materials Category posted on the ChemRTK HPV Challenge Program Web site on August 22, 2002. I commend The American Petroleum Institute for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that The American Petroleum Institute advise the Agency, within 90 days of this posting on the Web site, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the HPV Challenge Program Web site "Submit Technical Questions" button or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

-S-

Oscar Hernandez, Director

Risk Assessment Division

Enclosure

cc: C. Auer
A. Abramson
W. Penberthy
M. E. Weber

**EPA Comments on Chemical RTK HPV Challenge Submission:
Waxes and Related Materials**

SUMMARY OF EPA COMMENTS

The sponsor, the American Petroleum Institute, submitted a test plan and robust summaries to EPA for Waxes and Related Materials dated August 6, 2002. EPA posted the submission on the ChemRTK HPV Challenge Web site on September 22, 2002. The category consists of the refinery streams and finished products involved in the production of petroleum waxes and related materials consisting of eight complex mixtures of C₁₂-C₈₅ hydrocarbons that are further divided into 3 subcategories: slack wax, refined wax, and petrolatum.

EPA has reviewed this submission and has reached the following conclusions:

1. Category Justification. EPA agrees with the grouping of the waxes and related materials processed from the selected petroleum refinery streams by successive processing steps that separate the wax and oil portions.
2. Physicochemical Properties and Environmental Fate. The submitter needs to provide vapor pressure data for all category members, boiling point data for slack wax and petrolatum, and biodegradation data for petrolatum, because in Table 3 of the test plan these fields have been designated "Adequate."
3. Health Effects. EPA agrees with the submitter's test plan to conduct a bacterial gene mutation test and a combined repeated-dose/reproduction/developmental toxicity screening test using slack wax. The latter testing will also include an *in vivo* evaluation of erythrocyte micronucleus formation.

4. Ecological Effects. EPA agrees with the submitter's technical discussion on the toxicity and physicochemical property information on waxes and related materials that adequately describes low acute and chronic toxicity to aquatic organisms. However, data indicating that no toxicity is expected from these chemicals referenced from CONCAWE, 1997 should be brought forward to support the statement and enhance the technical discussion.

EPA requests that the submitter advise the Agency within 90 days of any modifications to this submission.

EPA COMMENTS ON THE WAXES AND RELATED MATERIALS CHALLENGE SUBMISSION

Category Definition

The category consists of eight substances defined by their physicochemical properties and the degree of processing and corresponding reduction in oil content and impurities. These substances mainly consist of complex mixtures of normal paraffin and cycloparaffin waxes ranging in carbon number from C₁₂ to C₈₅, with the majority of these hydrocarbons being greater than C₂₀. These substances also contain varying amounts of residual or added oil consisting of mainly alkylated aromatic hydrocarbons, but may also contain polynuclear aromatic hydrocarbons (PAHs). These substances are further divided into the following three subcategories:

Sub-category	CAS No.	Substance
<u>Slack Waxes</u>	64742-61-6	Slack wax (Petroleum)
<u>Refined/finished Waxes</u>		
(Paraffin)	8002-74-2	Paraffin Waxes and hydrocarbon waxes
	64742-43-4	Paraffin waxes (petroleum), clay treated
	64742-51-4	Paraffin waxes (petroleum), hydrotreated
(Microcrystalline)	63231-60-7	Paraffin waxes and hydrocarbon waxes, microcrystalline
	64742-42-3	Hydrocarbon waxes (petroleum), clay treated, microcrystalline
	64742-60-5	Hydrocarbon waxes (petroleum), hydrotreated, microcrystalline

Slack Wax is composed of C₁₂ to C₈₅ hydrocarbons, 2 to 30 wt % oil and may have a very low content of alkylated aromatic hydrocarbons.

The test plan description of slack waxes (page 4) indicates that slack waxes are derived from solvent-refined vacuum distillates, in which case they contain a very low content of alkylated aromatic hydrocarbons. However, in the next paragraph, the submitter states that information on and analysis of vacuum residuum samples indicate that aromatic contents range from 34.7 to 65.0 wt % and this would represent the “worse case” with regard to aromatic content of slack wax. The submitter needs to clarify this information as it appears contradictory with respect to alkylated and/or aromatic hydrocarbons contents.

Refined/finished waxes are produced by deoiling slack wax including reducing the amount of PAHs. They are classified as either paraffin waxes (lower melting paraffin waxes) or microcrystalline waxes (high melting waxes). The paraffin waxes contain C₁₈-C₇₅ hydrocarbons (mainly n-alkanes with lesser amounts of isoalkanes and cycloalkanes) and <2.5 wt % oil. The microcrystalline waxes contain C₂₃-C₈₅ hydrocarbons (mainly isoalkanes and cycloalkanes) and <5 wt % oil, with trace amounts of alkylated aromatic hydrocarbons.

Further purification of refined waxes and addition of greater than 10% USP grade white mineral oil results in Petrolatum (Petroleum Jelly).

Category Justification

Overall, EPA agrees with the submitter’s support of the category members based on the common source and the known and reasonably anticipated similarities in physicochemical, environmental, and toxicological properties of these substances. The submitter’s selection of slack wax as a representative category member for further testing is also appropriate because it has a higher proportion of impurities and potentially toxic materials.

All category members are derived from the processing of the same refinery streams and contain varying ratios of two major components, wax and oil. Because the waxes are composed predominantly of hydrocarbons with carbon numbers typically greater than C₂₀ (C₁₂-C₈₅ overall range), these substances are expected to exist as semi-solids or solids, having low water solubilities and vapor pressures, and limited bioavailability, environmental distribution, and degradation. These expectations are reasonable for the wax components of the substances and are generally supported by the weight-of-evidence provided by the submitter. However, the submitter needs to discuss whether the same expectations extend to the oil components of the waxes; whether the carbon number range given for the wax components also includes the range for the oil components; and whether these non-wax

hydrocarbons will have similar physicochemical and environmental properties. Although the health effects data support the category for the wax fraction of the substances, additional data may be necessary to support the oil fraction of the substances.

The submitter anticipates that the toxicological properties of these substances will be determined largely by the oil content of the substances, attributing the expected toxicities to the aromatic and olefinic hydrocarbons in the oil. Therefore, following processing steps, the toxicity of the substances is expected to decrease as the oils and other impurities are removed from the waxes. Slack waxes, therefore, define the upper range in expected toxicities of the substances in the category. EPA agrees with the submitter's assertion, but notes that supporting toxicological evidence for oils was omitted from the submission. However, the submitter indicated that materials similar to the base oil component of slack waxes are included in the Lubricating Oil Basestocks and Aromatic Extracts HPV test plans and will provide supplementary data for oil and aromatic components of the materials in the waxes category.

EPA notes that the toxicological data do not support the submitter's inclusion of paraffin (low melting point) and microcrystalline wax (high melting point) in a single subgroup of refined/finished waxes. In general, paraffin wax appeared to be more toxic than microcrystalline wax. Microcrystalline wax was relatively non-toxic to rats, causing only minor effects at the highest dose of 2000 mg/kg/day, whereas the paraffin wax caused lymph node lesions at \$2 mg/kg/day and a multiplicity of effects at \$200 mg/kg/day (increased liver and spleen weights, hematological changes, and histopathology of the liver, small intestine, and cardiac mitral valve). On the basis of toxicological differences, the two types of finished waxes would be more appropriately assigned to separate subgroups.

Test Plan

The tested refined/finished waxes need to be defined according to subgroup criteria listed in Table 2 of the test plan. For example, on page 12 of the test plan the submitter provides biodegradation information for an intermediate wax (CAS # 97489-05-9), and in the robust summary (page 16) it provides data on slack wax (petroleum), hydrotreated (CAS # 92062-09-4). These two CAS numbers are not mentioned in the category table on page 4 of the test plan.

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility).

The data for melting point, partition coefficient, and water solubility are adequate for the purposes of the HPV Challenge Program.

Boiling Point. The boiling point data for paraffin and microcrystalline waxes are adequate for the purposes of the HPV Challenge Program. In Table 3 of the test plan (page 14) the submitter indicated that adequate data are available for all category members; however, it did not provide any data in the robust summaries for slack waxes and petrolatum. The submitter needs to provide these data if available.

Vapor Pressure. The submitter needs to provide the vapor pressure data as indicated in Table 3 of the test plan.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity).

The data for photodegradation and stability in water are adequate for the purposes of the HPV Challenge Program

Biodegradation. In Table 3 of the test plan (page 14) the submitter indicated that adequate data are available for all category members; however, it did not provide any data in the robust summaries for petrolatum. The submitter needs to provide these data if available.

In the robust summary, on pages 7, 9 and 16 respectively, the submitter indicates that paraffin wax, microcrystalline wax, and slack wax are inherently biodegradable. However the methods used by the submitter are modified OECD 301B, for paraffin wax and microcrystalline wax, and 301F, for slack wax, that are used to assess ready biodegradability. The submitter needs to clarify this discrepancy.

Fugacity. The sponsor estimated the fugacity of these chemicals using a Level I model. Although EPA had previously recommended the use of EQC Level I, this model is somewhat limited. EPA now recommends the use of EQC level III, which provides a more rigorous level of analysis. The submitter also did not provide the assumptions and data inputs used to develop its fugacity estimates. The submitter needs to provide these.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

Slack Wax. Acute toxicity data are not available for slack wax. The submitter reasonably argued that the toxicity of slack waxes would result from the combined effects of the component waxes and oils. Wax toxicity would be represented by extrapolation from the data submitted for the refined/finished waxes, whereas the base oil portion will be represented by extrapolation from data contained in the Lubricating Oil, Basestocks and Aromatic Extracts test plans HPV submission. The submitter has proposed a combined repeated-dose/reproduction/developmental toxicity screening test (OECD TG 422) using slack wax. In addition, the submitter has proposed testing of slack wax for bacterial gene mutations (OECD TG 471) and in vivo mammalian erythrocyte micronucleus formation (OECD TG 474). The micronucleus test will be conducted on the repeated-dose test

animals from the above OECD TG 422 study. EPA believes that the submitter's strategy of testing slack waxes as the most toxic subgroup and extrapolating data to the other subgroups is reasonable.

Refined/Finished Waxes. Although the submitter provided data for acute and repeated-dose toxicity endpoints, EPA reserves judgement on their adequacy until the submitter provides adequate robust summaries. The adequacy of these data could not be determined because a single summary was submitted for a total of nine substances that were tested in a series of three studies. The robust summary did not adequately define the test materials; the submitter needs to provide the missing information in separate repeated-dose toxicity robust summaries. For the reproductive toxicity endpoint, the submitter needs to provide relevant information on histopathology of male and female reproductive organs for petrolatum and refined waxes that may be available in the repeated-dose toxicity studies. This information will assist in the evaluation of the appropriateness of the data extrapolated from slack waxes. Data for genetic toxicity and reproduction/developmental endpoints are not available; however, EPA believes that these endpoints will be addressed by the data for slack wax.

Petrolatum. Adequate data on the acute and repeated-dose toxicity endpoints are available for petrolatum. Although data for genetic toxicity and reproduction/developmental endpoints are not available, EPA believes that these endpoints will be addressed by the data for Slack Wax.

Ecological Effects (fish, invertebrates, and algae).

No ecotoxicity robust summaries were provided, and the submitter proposed no ecotoxicity testing on any of the category chemicals.

The test plan contains a technical discussion on the physicochemical property and toxicity information in lieu of testing. The discussion concludes that these chemicals are not expected to have acute and chronic effects in aquatic organisms and cited work by Adema and van den Bos Bakker (1986) and CONCAWE (1997). Although EPA agrees with the submitter that these chemicals may pose low or no hazard to aquatic organisms, it reserves judgement on the adequacy of the statements in the test plan pending submission and evaluation of robust summaries for the cited studies.

Specific Comments on the Robust Summaries

Physicochemical Properties

Melting Point. The submitter needs to incorporate the melting point data presented in section 2.12 of the robust summary into MELTING POINT Section 2.1. The melting point

data need to be provided in robust summary format showing the method and source of the information.

Health Effects

Repeat Dose Toxicity. Two robust summaries were reviewed.

A single robust summary described three 90-day GLP/OECD guideline toxicity assays for several kinds of refined/finished waxes in dietarily-exposed rats. The summary was inadequate because of poor organization (merging discussion of the different studies), omissions, and inclusion of extraneous information (on high-sulfur waxes). The summary did not define the tested materials, so it is not possible to determine whether they met the wax type criteria (page 22 indicated that the wax characteristics were published elsewhere and page 23 indicated that the tabular data referred to follow-up studies, apparently not the main study). Other omissions for the main study included: the statistical methods, the organs evaluated for histopathology, the minor treatment-related effects observed in high-dose animals exposed to high melting point wax at the high dose, and information on the statistical significance of the observed hematological changes in rats exposed to low melting point wax. The latter two omissions raise uncertainty as to the NOAEL/LOAEL values for this study. The methods section for a hydrocarbon distribution assay, carried out on satellite groups, did not specify the detection methods or the tissues and hydrocarbons that were assayed. In the Remarks section of this summary, tabular data were given for a follow-up study, with NOAEL values, but the results of this study were not described.

Followup Activity

EPA requests that the submitter advise the Agency within 90 days of any modifications to this submission.